

**AMENDMENTS TO THE CLAIMS:**

Please incorporate the following amendments into the claims of the subject application.

1-33. (canceled)

34. **(currently amended)** The method of claim 69 or 77 wherein the compound is determined to be a compound that reduces the activity of an active receptor state of said constitutively activated GPCR.

35-44. (canceled)

45. **(currently amended)** The method of claim 69 or 77 wherein the third intracellular loop of the endogenous GPCR ~~of step (a)~~ comprises the following sequence:

X1BBHyX2

wherein X1 is an amino acid; B is a basic amino acid; Hy is a hydrophobic amino acid; and X2 is an amino acid.

46. (original) The method of claim 45 wherein X1 is glycine.

47. (original) The method of claim 45 wherein X1 is lysine.

48. (original) The method of claim 45 wherein Hy is alanine.

49. (original) The method of claim 45 wherein X2 is lysine.

50. (original) The method of claim 45 wherein X2 is arginine.

51. (original) The method of claim 45 wherein X2 is glutamic acid.

52. **(currently amended)** The method of claim 69 or 77 wherein the second intracellular loop of the endogenous GPCR ~~of step (a)~~ comprises the following sequence:

XRY

wherein X can be any amino acid other than aspartic acid; R is arginine; and Y is tyrosine.

53-60. (canceled)

61. (original) The method of claim 45 wherein the sequence XIBBH<sub>2</sub>Y is an endogenous sequence.

62. (original) The method of claim 52 wherein the sequence XRY is an endogenous sequence.

63-68. (canceled)

69. **(currently amended)** A method for directly identifying a non-endogenous candidate compound as a compound that stimulates an endogenous G protein coupled receptor (GPCR) or reduces the activity of an active receptor state of an endogenous GPCR, ~~wherein said endogenous GPCR has been associated with a disease or disorder in a mammal and wherein an endogenous ligand for said endogenous GPCR has not been identified~~ **and wherein said endogenous GPCR comprises a mutation in its amino acid sequence so as to render it constitutively active**, said method comprising the steps of:

(a) ~~subjecting said endogenous GPCR to constitutive receptor activation to create a constitutively activated GPCR;~~

~~(b)~~ contacting the non-endogenous candidate compound with said constitutively activated GPCR;

[(c)] **(b)** determining whether said non-endogenous candidate compound is a compound that stimulates said endogenous GPCR or reduces the activity of an active receptor state of said endogenous GPCR, by measuring the ability of the **candidate** compound to stimulate or inhibit functionality of said constitutively activated GPCR, respectively.

70-76. (canceled)

77. **(currently amended)** A method for directly identifying a non-endogenous ~~candidate~~ compound with compound efficacy as to an endogenous orphan GPCR, the method comprising the steps of:

- (a) subjecting said endogenous orphan GPCR to constitutive receptor activation to create a constitutively activated orphan GPCR;
- (b) contacting the constitutively activated orphan GPCR with the non-endogenous compound;
- (c) comparing the functionality of the constitutively activated orphan GPCR in the presence and absence of the non-endogenous compound; and
- (d) identifying the non-endogenous compound as having compound efficacy if the presence of the compound measurably alters the functionality of the endogenous constitutively activated orphan GPCR as compared to the functionality of the endogenous constitutively activated orphan GPCR in the absence of the compound.

78. (canceled)

79. **(currently amended)** The method of claim 77 ~~or 78~~, wherein said functionality of the constitutively activated orphan GPCR is binding to GTP.

Please add the following claim:

80. **(new)** The method of claim 77, wherein said constitutively activated orphan GPCR comprises a mutation in its amino acid sequence so as to render it constitutively active.